May 10, 2001

Elmer Rauckman, Ph.D.
Trioxane HPV Consortium
One Rowlands Road
Flemington, NJ 08822

Dear Dr. Rauckman:

The Office of Pollution Prevention and Toxics is transmitting EPA s comments on the robust summaries and test plan for Trioxane (CAS No. 110-88-3), posted by EPA on January 12, 2001. I commend the Trioxane Manufacturers Consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

The Consortium supplied information that on a weight-of-evidence basis satisfies the reproductive toxicity testing criteria under the HPV Challenge Program. EPA agrees with the Consortium s conclusion that for priority-setting purposes no new reproductive toxicity tests are necessary, but our reasoning is different, as explained in the comments.

The Consortium needs to supply information missing from the ecotoxicity robust summaries, the assumption and data inputs to the fugacity model, and clarifications to certain health robust summaries.

As with other submissions where the available data are either inadequate or insufficiently documented, this case will remain open until adequate documentation is in hand.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that the Consortium advise the Agency, within 60 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
M. E. Weber
A. Abramson

EPA Comments on Chemical RTK HPV Challenge Submission:

Trioxane

SUMMARY OF EPA COMMENTS

The sponsor, the Trioxane Manufacturers Consortium, submitted a Test Plan and Robust Summaries to EPA, dated December 28, 2000, for Trioxane (CAS No. 110-88-3). EPA posted the submission on the ChemRTK HPV Challenge Web site on January 12, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. Robust summaries are adequate, except that for the fugacity model, the sponsor needs to provide the assumption and data inputs to the model.

2. Health Endpoints: Appropriate SIDS-level tests have been performed for all health endpoints. Several robust summaries need to be enhanced for clarity (see specific comments below).

3. Ecotoxicity. The robust summaries are adequate, except for a few missing data elements for several endpoints (see specific comments below).

EPA is requesting that the Sponsor advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE TRIOXANE CHALLENGE SUBMISSION

TEST PLAN

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

Adequate existing data are available for these endpoints.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution).

Adequate existing data are available for these endpoints.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate existing data are available for these endpoints. The information presented for the reproductive toxicity endpoint two dominant-lethal tests and an ovarian function test in rats would not normally satisfy the SIDS-level assessment for this endpoint. However, in this case, the dominant lethal study exceeded normal test guidelines (including a longer exposure period and histopathology of the testes) and demonstrated effects on the male reproductive organs. Therefore, EPA agrees with the conclusion of the sponsor that no new reproductive toxicity tests are necessary, but for different reasons. EPA believes that accepting the unusual dominant-lethal study protocol followed for trioxane plus a developmental toxicity study is consistent with current OECD SIDS policy that an existing 90-day subchronic study with evaluation of male reproductive organs plus a developmental toxicity study satisfy the reproductive

toxicity endpoint for a screening-level (SIDS-level) analysis.

Ecological Effects (fish, invertebrate and algal toxicity).

Adequate existing data are available for these endpoints. In the algal study the chemical concentration did not reach the appropriate level (1000 mg/L) for the limit test. However, the sponsor supplied other information, including reference to a supporting study performed at higher concentration and a predicted toxicity value generated with ECOSAR. Considering the totality of the information available, generating additional data in this case would not be likely to improve the understanding of this endpoint for trioxane.

SPECIFIC COMMENTS ON ROBUST SUMMARIES

Fate

For the fugacity model, the sponsor needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation).

EPA recommends using the EQC Level III model from the Canadian Environment Modeling Centre at Trent University, which allows full control of data inputs. This model can be found at the following Web address: http://www.trentu.ca/academic/aminss/envmodel/.

Health Effects

Acute Dermal Toxicity (p.58): The robust summary for the acute dermal toxicity study contains supporting information that appears to be a typographical error (page 59, under Other , the LD50 is likely 1500 mg/kg, not 1500 g/kg).

Mouse lymphoma forward mutation assay (p. 78): The summary should be enhanced to provide the mutational frequencies of the positive control (DMN) in the two activation experiments.

Ecotoxicity Studies

Robust summaries were submitted for fish, invertebrate and algal studies. The following EPA comments reflect the information in the robust summaries (the full study report may address these comments):

EPA evaluated each robust summary and determined that all studies appear adequate. Some deficiencies in the summaries are: dissolved oxygen (DO) and total organic carbon (TOC) are not reported in the fish summary; TOC and temperature are not reported in the invertebrate summary. The sponsor needs to include the missing information in the summaries; see EPA s HPV Challenge Program Guidance (http://www.epa.gov/opptintr/chemrtk/guidocs.htm).

Fish, daphnia, and algae predicted values from ECOSAR were provided to support the measured aquatic toxicity data for each of these end points. The estimated values support the measured data. Using SAR to support measured data in this manner is appropriate and consistent with the EPA Challenge guidance for applying structure-activity relationships (http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm).

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.